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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/594,164

09/26/2006

Takashi Sugioka

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EXAMINER

CLARK, SARA E

ART UNIT

PAPER NUMBER

1612

NOTIFICATION DATE

DELIVERY MODE

06/24/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/594,164	<b>Applicant(s)</b> SUGIOKA ET AL.	
	<b>Examiner</b> SARA E. CLARK	<b>Art Unit</b> 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 March 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-8 and 10-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-8 and 10-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***NON-FINAL REJECTION***

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 3/10/2010.

Claims 2, 9, and 13-18 are canceled.

Claims 1 and 8 have been amended.

No new claims have been added.

Thus, claims 1, 3-8, and 10-12 now represent all claims currently pending and under consideration.

***REQUEST FOR CONTINUED EXAMINATION***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/19/2010 has been entered.

***INFORMATION DISCLOSURE STATEMENT***

No new Information Disclosure Statements (IDS) have been submitted.

***WITHDRAWN REJECTIONS***

Rejections under 35 USC §112

Due to the amendments to the claims, the rejection of claims 1-18 under 35 USC 112, second paragraph, for indefiniteness, is withdrawn.

Due to the amendments to the claims, the rejection of claims 1-18 under 35 USC 112, first paragraph, for lack of written description, is withdrawn.

### ***MAINTAINED REJECTIONS***

The following rejection is maintained from the previous Office Action dated 12/10/2009, on the ground that the references cited therein continue to read on the limitations of the amended claims.

#### Rejections under 35 USC §103

Claims 1, 3-8, and 10-12 stand rejected under 35 USC 103(a) as obvious over Nakazawa and Moriarty.

### ***RESPONSE TO ARGUMENTS***

Applicant's arguments filed 3/10/2010 have been fully considered but they are not persuasive. Specifically, Applicant contends that the references do not teach or suggest protection of the 21-hydroxyl group while leaving the 7-hydroxyl group unprotected, (Remarks, p. 11); that a skilled artisan would not be motivated to modify Nakazawa in view of Moriarty, because compound 5 of Moriarty has a 7-oxo group rather than a 7-hydroxyl group, which serves as an intramolecular proton donor for the

Birch reduction (Remarks, pp. 11-12); and that the references fail to appreciate or recognize the unexpected result of improved yield when the 21-hydroxyl group is protected.

However, Nakazawa et al. disclose the claimed process using the unprotected 7,21-hydroxyl species of the claimed compounds; protection of the 21-hydroxyl group *following* the reduction reaction (para. 22); and TBDMS as a suitable hydroxyl-protecting group (para. 0042).

The only feature of the claimed invention Nakazawa does not disclose is protection of the 21-hydroxyl group *preceding* the reduction reaction, followed by deprotection.

Moriarty discloses protection of a 24-hydroxyl group with TBDMS preceding a Birch reduction reaction with lithium in liquid ammonia. Moriarty is cited as evidence that a skilled artisan would have a reasonable expectation that the claimed reaction would run in the presence of a TBDMS 21-hydroxyl-protecting group, regardless of the reasons contemplated by Moriarty for introducing it.

Applicant contends that the obviousness rejection is overcome by evidence of unexpected results, namely, that the reaction of Nakazawa modified by protecting the 21-hydroxyl group of the starting material achieves almost quantitative yields (95% for reduction of the pregna-1,4-diene, Example 1; and 96% for reduction of the pregn-4-ene, Example 2), whereas the C<sub>5</sub>-C<sub>6</sub> double bond of compound 5 of Moriarty is reduced in only 81% yield (Remarks, p. 14).

Adjusting these yields to account for the deprotection step (Example 3), the claimed process results in a final yield of  $95\% \times 95\% = 90.25\%$  (starting with the pregna-1,4-diene) and  $96\% \times 95\% = 91.2\%$  (starting with the pregn-4-ene). Thus, the claimed process increases the yield over Moriarty by about 10%. However, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In addition, while the specification discusses the principle of protecting the 21-hydroxy group in general (p. 3, line 24 to p. 4, line 8), there is no example directly comparing the identical process under identical conditions, wherein one starting material has a protected 21-hydroxyl group and the other has an unprotected 21-hydroxyl group.

Finally, evidence of unexpected results must be commensurate with the scope of the claims. As recognized by MPEP §716.02(d),

Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980).

Because claims 1, 3, 6-8, and 10 recite any hydroxyl-protecting group, claims 1-5, 8, and 10-12 recite any alkali or alkaline earth metal, and claims 1, 3-8, and 10-12 recite any proton donor, it would be unreasonable to conclude that the data presented in Examples 1 and 2 supports a finding of unexpected results commensurate with the

scope of the claims sufficient to overcome the *prima facie* case of obviousness. For these reasons, the rejection under 35 USC 103 of claims 1, 3-8, and 10-12 is maintained.

### ***NEW REJECTIONS***

#### ***Claim Rejections - 35 USC § 112, First Paragraph***

##### ***Written Description - New Matter***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3-8, and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Specifically, claims 1 and 8 recite a metal “present in an amount of 1.4-4 molar equivalents” and “present in an amount of 2.8-8 molar equivalents” relative to the compound of formula (I). The disclosure, arguments, and supporting documentation (Bansal, 1996) do not provide adequate support for this limitation, which relate to the theoretically required amount of metal (electron source) required to reduce a carbon-carbon double bond, rather than the actual amount required in practice, which can vary substantially from the theoretical amount required.

For example, USPN 7,008,940 teaches that a Birch reduction with an alkali metal in liquid ammonia is carried out with about 1 to about 20 (molar) equivalents, preferably about 1 to about 5 (molar) equivalents of the alkali metal, such as sodium or lithium (col. 34, lines 32-58).

In addition, the amended specification discloses that the amount of the alkali metal to be used is "generally within the range of 0.7 to 2 times the amount necessary for reducing the carbon-carbon double bond of compound (I) to be reduced" (specification p. 13, lines 10-13), which amount is not disclosed with any specificity in the specification, original claims, or supporting documentation.

As recognized by MPEP §706.03(o), "[n]ew matter includes not only the addition of wholly unsupported subject matter, but may also include adding specific percentages or compounds after a broader original disclosure, or even the omission of a step from a method." See MPEP § 608.04 to § 608.04(c).

### **CONCLUSION**

Claims 1, 3-8, and 10-12 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Art Unit: 1612

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/  
Examiner, Art Unit 1612

/Frederick Krass/  
Supervisory Patent Examiner, Art Unit 1612